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118 same (crown ether)	8

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118 same (crown ether)

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Entry 4 of 8

File: USPT

Dec 16, 1997

DOCUMENT-IDENTIFIER: US 5698405 A

TITLE: Method of reducing immunogenicity

BSPR:

Preparation of protein, biotin or avidin/streptavidin (molecule) conjugated to a magnetic resonance image enhancing agent can be effected by a variety of methods. In order to load a molecule with a large number of paramagnetic ions, it may be necessary to react it with a reagent having a long tail to which are attached a multiplicity of chelating groups for binding the ions. Such a tail can be a polymer such as a polylysine, polysaccharide, or other derivatized or derivatizable chain having pendant groups to which can be bound chelating groups such as, e.g., ethylenediaminetetraacetic acid (EDTA), diethylenetriaminepentaacetic acid (DTPA), porphyrins, polyamines, crown ethers, bis-thio-semicarbazones, polyoximes, and like groups known to be useful for this purpose. The chelate is normally linked to the molecule by a group which enables formation of a bond to the molecule with minimal loss of immunoreactivity and minimal aggregation and/or internal cross-linking. Other, more unusual, methods and reagents for conjugating chelates to antibodies are disclosed in U.S. Pat. No. 4,824,659 to Hawthorne, entitled "Antibody Conjugates", issued Apr. 25, 1989, the disclosure of which is incorporated herein in its entirety by reference.

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Entry 2 of 17

File: USPT

Dec 22, 1998

DOCUMENT-IDENTIFIER: US 5851527 A

TITLE: Method for antibody targeting of therapeutic agents

BSPR:

Still another approach is to use a carrier polymer that bears the drugs, chelators, boron addends or other agents and that has a high attraction for the target, in unmodified form, but which is then modified by conjugation to solubilizing substrate molecules which are then cleaved by targeted enzyme. One illustration of this subgeneric type of substrate-agent conjugate is a polylysine to which are bound a plurality of radiometal or paramagnetic metal chelators, carboranes or MTX molecules. This carrier conjugate is then condensed with a plurality of short dextran oligomers, e.g., by Schiff base formation with lightly oxidized dextran and borohydride stabilization, in a ratio which increases the solubility (reduces the "stickiness") of the polylysine and makes it readily transportable in serum and readily diffusable through capillary walls (and then loaded with radioisotope or paramagnetic ions, if chelators are attached to the carrier). At a target site, e.g., a tumor, a localized antitumor antibody-dextranase conjugate would strip off the dextran coating from the polylysine to a sufficient extent to make it "sticky" again, whereupon it would adhere to the tumor cells and the bound polylysine, bearing its loading of diagnostic or therapeutic agent would then act upon the tumor cell to permit imaging or cytotoxic therapy.

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Entry 8 of 33

File: USPT

Jul 13, 1999

DOCUMENT-IDENTIFIER: US 5922859 A

TITLE: Complexes containing nucleic acid which can be taken-up by endocytosis into higher eukaryotic cells

BSPR:

Another series of tests were carried out on the principle of using a sub-optimum quantity of the particular conjugate, once the optimum ratio of conjugate to DNA was known, mixing the conjugate with increasing amounts of free (not covalently bound) polycation or a substance of polycationic nature (polylysines of various levels of polymerization and protamines and the histones H1, H3 and H4 were used), and adding the resulting mixture to a constant amount of DNA. The transfection efficiency of the complexes, which was significantly below the optimum transfection level when the sub-optimum quantity of conjugate was used, could be fully restored or even exceeded by the addition of free polycation. Only spermidine and spermine, which were known to condense DNA only at a low ionic strength (Tikchonenko et al., 1988) were unable to increase the expression of DNA under the physiological conditions for the tissue culture system.

BSPR:

Following the titration experiments to determine the optimum ratios of transferrin to polycation, investigations were carried out on the molecular state of the complexes which were formed under conditions of optimum DNA/conjugate ratios. The aim of these investigations was to examine whether the change in the conjugation ratios affected the higher order structure of the complexes. For this purpose, transferrin-polycation-plasmid-DNA complexes, prepared analogously to the method used for transferrinfection, were examined under the electron microscope. The electron microscopic analysis surprisingly showed that the plasmid DNA in the presence of the conjugates appears compressed into toroidal structures (like doughnuts) with a diameter of about 80 to 100 nm, irrespective of the method of preparation for electron microscopy. The surprising feature of these results was that the doughnut structures, obtained with those conjugates which had proved most efficient in the transferrinfection, conformed to the structure of complexes between DNA and free polylysine, i.e. the ability of polylysine to condense DNA had not been affected by the fact that it was coupled to an internalizing factor. The condensation of .lambda.-DNA by polylysine at high salt concentrations (Laemmli, 1975) or by spermidine at a very low ion intensity (Chattoraj et al., 1978) was known from the literature.

BSPR:

The results of the tests carried out have led to the assumption that the increase in expression brought about by the free bonding factor obviously cannot be attributed, or at least not exclusively, to DNA compacting, but possibly, in addition, to a protective action for the DNA and hence an inhibition of DNA breakdown in the cell and/or a positive influence on the exposure of the nucleic acid to the machinery of expression.

BSPR:

The substances of group a) include succinylacetone, while the increase in the number of transferrin receptors can probably be attributed to the inhibition of protoporphyrin IX biosynthesis. The substances of group b) include those which induce an iron deficiency in the cell, e.g. the iron chelate forming agent desferrioxamine, which presumably causes an increase in the number of transferrin receptors because the conversion of protoporphyrin IX into heme is prevented. Fundamentally, all the substances, particularly iron chelating agents, which can be absorbed into the cell and which have the effect of desferrioxamine on the quantity of iron available for heme formation, are suitable for increasing the number of transferrin receptors.

ORPL:

Laemmli, U.K., "Characterization of DNA condensates induced by poly(ethylene oxide) and polylysine," Proc. Natl. Acad. Sci. USA 72:4288-4292 (1975).

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Document Number 21

Entry 21 of 33

File: USPT

Feb 3, 1998

US-PAT-NO: 5714166

DOCUMENT-IDENTIFIER: US 5714166 A

TITLE: Bioactive and/or targeted dendrimer conjugates

DATE-ISSUED: February 3, 1998

US-CL-CURRENT: 424/486, 424/1.29, 424/1.33, 424/1.37, 424/1.41, 424/1.49,
424/178.1, 424/193.1, 424/204.1, 424/234.1, 424/405, 424/417, 424/78.08,
424/9.3, 424/9.32, 424/9.322, 424/9.36, 424/9.4, 424/9.42, 424/9.6,
424/93.1, 424/DIG.16, 514/772, 523/105, 525/417

APPL-NO: 8/ 400203

DATE FILED: March 7, 1995

PARENT-CASE:

CROSS REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of our applications Ser. No. 316,536, filed Sep. 30, 1994, now abandoned which is a continuation-in-part of our application Ser. No. 207,494, filed Mar. 7, 1994, now abandoned which is a divisional and continuation-in-part of application Ser. No. 043,198, filed Apr. 5, 1993, now U.S. Pat. No. 5,527,524, issued Jun. 18, 1996, which is a continuation-in-part of application Ser. No. 654,851, filed Feb. 13, 1991, now U.S. Pat. No. 5,338,532, issued Aug. 16, 1994, which is a continuation-in-part of application Ser. No. 386,049, filed Jul. 26, 1989, now abandoned, which is a continuation-in-part of application Ser. No. 087,266, filed Aug. 18, 1987, now abandoned, which is a continuation-in-part of application Ser. No. 897,455, filed Aug. 18, 1986, now abandoned. All of these prior application documents are hereby incorporated by reference in their entireties herein.

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polychelator	10

Database: All Databases (USPT + EPAB + JPAB + DWPI + TDBD) ▼**Refine Search:**

polychelator ▲▼

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Entry 1 of 10

File: USPT

Nov 5, 1996

US-PAT-NO: 5571940

DOCUMENT-IDENTIFIER: US 5571940 A

TITLE: Method for making conjugate moieties capable of chelating paramagnetic metals and designed for coupling with a factor responsive to specific cellular marker sites

DATE-ISSUED: November 5, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Palacios; Paul	Madrid	N/A	N/A	ESX

US-CL-CURRENT: 562/556; 534/797, 548/318.1, 548/319.1, 548/319.5,
562/426, 562/555, 562/561, 562/564, 562/565

CLAIMS:

I claim:

1. Polyalkylaminopolycarboxylic chelatants having a reactive end group

X.sup.1 for coupling to proteins and having formula III

X.sup.1 --Alk--NH--(CO--CH--NH).sub.n --MY Z-NH-MY (III)

where

X.sup.1 is a --CHO or --SH group;

Alk is a C.sub.1 to C.sub.4 alkylene, optionally interrupted by a --S-- bond;

Z is a C.sub.1 to C.sub.4 alkylene, optionally interrupted by a --COO-- bond;

at least one Y represents a polyalkyleneamino-polycarboxylic acid chelatant molecule, the other Y being either in its free acid form or as complex with paramagnetic ions;

n is an integer from 0 to 100; and

M represents a link between --NH and Y, said link being either an amido bond involving a --CO of Y and said --NH of III, or an organic bridging substituent connecting to an alkylene carbon of Y, said bridging substituent resulting from bridging functional groups selected from the group consisting of isocyanato-, isothiocyanato-, bromoacetamido-, diazo-, N-hydroxysuccinimide esters and intermolecular or intramolecular anhydrides-.

2. Chelatants according to claim 1, having the formulae

HOC--CH.sub.2 --S--(CH.sub.2).sub.2 --NHCOCH.sub.2 [N(AcOH) (CH2).sub.2]
].sub.2 --N(AcOH).sub.2

and ##STR9## wherein n is 50-100.

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